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EXAMINER
WHISENANT, ETHAN C

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/023,337	VISION ET AL.	
	Examin r	Art Unit	
	Ethan Whisenant, Ph.D.	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- *Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed* after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,20,21,28,29 and 37-42* is/are rejected.

7)☒ Claim(s) *18,19,22-27 and 30-36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

NON-FINAL ACTION

SEQUENCE RULES

1. This application complies with the sequence rules and the sequences have been entered by the Scientific and Technical Information Center.

35 USC § 112- 2ND PARAGRAPH

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

CLAIM REJECTIONS under 35 USC § 112- 2ND PARAGRAPH

3. **Claim(s) 10 and 12** is/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is confusing because it is attempting to recite a list of genetic diseases however, one member of the Markush group is not genetic disease (i.e. HLA typing) Please clarify.

Claim 12 is confusing because it is attempting to recite a list of gene however, some members of the Markush group are not genes but rather types of cancer disease (e.g. melanomas and osteosarcoma). Please clarify.

35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless --
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> **(e)** The invention was described in –
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)

CLAIM REJECTIONS UNDER 35 USC § 102

5. **Claim(s) 1-4, 9-17, 28-29, 40-41** is/are rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al. [US 6,060,288 (2000)].

Claim 1 is drawn to a method of detecting a target nucleic acid molecule in a sample which method comprises six required steps, including a step wherein an immobilized polymerase extended portion of the target nucleic acid - said portion being complementary to a portion of the target nucleic acid molecule - is detected with a labeled detection probe which labeled detection probe comprises a nucleotide sequence like that of the target nucleic acid molecule (i.e. will specifically hybridize thereto).

Adams et al. teach a method of performing the amplification of a target nucleic acid molecule on solid supports. See the entire document, note at least for example, Columns 3-5, Column 4, lines 57-67, and Column 5 lines 13-22, and lines 58-67.

As regards the limitations recited in Claims 9-13 see especially Column 5 lines 58-67. As regards the limitations recited in Claim 14 see especially Column 1, line 57- Column 2, line 3. Note also Column 7, line 18 - Column 9, line 9. As regards the limitations recited in Claims 15-17, see Column 22 lines 47-67. As regards the limitations recited in Claim 28 see, at least for example, Column 6, line 67.

6. **Claim(s) 1-4, 7, 9-11, 14, 17, 28-29, and 40-41** is/are rejected under 35 U.S.C.102 (b) as being anticipated by Carson et al. [US 5,747,251 (1998)].

Carson et al. teach a method of performing the amplification of a target nucleic acid molecule on solid supports and describe numerous Possible applications of this invention which the authors teach include, but are not necessarily limited to(1) Diagnosis and typing of infectious diseases such as HIV, venereal disease, hepatitis, mycobacterial infections, etc.;(2) HLA typing for organ transplantation and autoimmune disease diagnosis;(3) Cancer diagnosis through oncogene detection (4) Diagnosis of genetic diseases;(5) Monitoring of inflammatory diseases by assessing quantitative cytokine gene expression. See the entire document, note especially, at least for example, Column 5, beginning at line 35, Column 4, lines 20-31, and Column 8, beginning at line 22.

35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 103

9. **Claim(s) 5** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. [US 6,060,288 (2000)] as applied to Claims 1 and 4 above and further in view of Hall et al. [US 5,475,098 (1995)].

Claim 5 is drawn to an embodiment of Claim 4 wherein the infectious disease is caused by a bacteria selected from a defined group which includes *E. coli*.

Adams et al. teach all of the limitations of Claim 5 except these authors do not explicitly teach detecting *E. coli* nucleic acids However, as evidenced by Hall et al. it was well known in the art at the time of the invention to detect *E. coli* nucleic acids in a biological sample using PCR and probes specific for the amplified *E. coli* nucleic acids. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to detect E. coli using the primers disclosed by Hall et al. in the method of Adams et al. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

10. **Claim(s) 5** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson et al. [US 5,747,251 (1998)] as applied to Claims 1 and 4 above and further in view of Pilkaytis et al. [US 5,652,106 (1997)].

Claim 5 is drawn to an embodiment of Claim 4 wherein the infectious disease is caused by a bacteria selected from a defined group which includes *Mycobacterium tuberculosis.*

Carson et al. teach all of the limitations of Claim 5 except these authors do not explicitly teach detecting *Mycobacterium tuberculosis* nucleic acids. Note that these authors do teach using their invention to detect mycobacterial infections. See Column 8 beginning at line 22. However, as evidenced by Pilkaytis et al. it was well known in the art at the time of the invention to detect *Mycobacterium tuberculosis* nucleic acids in a biological sample using PCR and probes specific for the amplified *Mycobacterium tuberculosis* nucleic acids. Therefore, absent an unexpected result it would have been

prima facie obvious to one of ordinary skill in the art at the time of the invention to detect *Mycobacterium tuberculosis* using the primers disclosed by Pilkaytis et al. in the method of Carson et al. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

11. **Claim(s) 6** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. [US 6,060,288 (2000)] as applied to Claims 1 and 4 above and further in view of Springer et al. [US 5,489,513 (1996)].

Claim 6 is drawn to an embodiment of Claim 4 wherein the infectious disease is caused by a fungal infectious agent selected from a defined group which includes *C. albicans.*

Adams et al. teach all of the limitations of Claim 6 except these authors do not explicitly teach detecting the nucleic acids of the fungal pathogen *C. albicans.* However, as evidenced by Springer et al. it was well known in the art at the time of the invention to detect *C. albicans* nucleic acids in a biological *sample* using PCR and probes specific for the amplified *C. albicans* nucleic acids. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to detect *C. albicans* nucleic acids using the primers disclosed by Springer et al. in the method of Adams et al. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

12. **Claim(s) 6** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson et al. [US 5,747,251 (1998)] as applied to Claims 1 and 4 above and further in view of Springer et al. [US 5,489,513 (1996)].

Claim 6 is drawn to an embodiment of Claim 4 wherein the infectious disease is caused by a fungal infectious agent selected from a defined group which includes *C. albicans*.

Carson et al. teach all of the limitations of Claim 6 except these authors do not explicitly teach detecting the nucleic acids of the fungal pathogen *C. albicans*. However, as evidenced by Springer et al. it was well known in the art at the time of the invention to detect *C. albicans* nucleic acids in a biological *sample* using PCR and probes specific for the amplified *C. albicans* nucleic acids. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to detect *C. albicans* nucleic acids using the primers disclosed by Springer et al. in the method of Carson et al. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

13. **Claim(s) 7** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. [US 6,060,288 (2000)] as applied to Claims 1 and 4 above and further in view of Respess [US 5,599,662 (1997)]

Claim 7 is drawn to an embodiment of Claim 4 wherein the infectious disease is caused by a viral infectious agent selected from a defined group which includes HIV.

Adams et al. teach all of the limitations of Claim 7 except these authors do not explicitly teach detecting the nucleic acid of the viral pathogen HIV. However, as evidenced by Respess it was well known in the art at the time of the invention to detect HIV nucleic acids in a biological sample using PCR and probes specific for the amplified HIV nucleic acids. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to detect HIV nucleic acids using the primers disclosed by Respess in the method of Adams et al. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to

make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

14. **Claim(s) 8** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. [US 6,060,288 (2000)] as applied to Claims 1 and 4 above and further in view of Wataya et al. [US 5,792,609 (1998)].

Claim 8 is drawn to an embodiment of Claim 4 wherein the infectious disease is caused by a parasitic infectious agent selected from a defined group which includes *P. falciparum*..

Adams et al. teach all of the limitations of Claim 8 except these authors do not explicitly teach detecting the nucleic acid of the parasitic infectious agent *P. falciparum.* However, as evidenced by Wataya et al. it was well known in the art at the time of the invention to detect *P. falciparum* nucleic acids in a biological sample using PCR and probes specific for the amplified *P. falciparum* nucleic acids. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to detect *P. falciparum* nucleic acids using the primers disclosed by Wataya et al. in the method of Adams et al. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

15. **Claim(s) 8** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson et al. [US 5,747,251 (1998)] as applied to Claims 1 and 4 above and further in view of Wataya et al. [US 5,792,609 (1998)].

Claim 8 is drawn to an embodiment of Claim 4 wherein the infectious disease is caused by a parasitic infectious agent selected from a defined group which includes *P. falciparum*..

Carson et al. teach all of the limitations of Claim 8 except these authors do not explicitly teach detecting the nucleic acid of the parasitic infectious agent *P. falciparum.* However, as evidenced by

Wataya et al. it was well known in the art at the time of the invention to detect *P. falciparum* nucleic acids in a biological sample using PCR and probes specific for the amplified *P. falciparum* nucleic acids. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to detect *P. falciparum* nucleic acids using the primers disclosed by Wataya et al. in the method of Carson et al. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

16. **Claim(s) 12** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson et al. [US 5,747,251 (1998)] as applied to Claims 1 and 11 above and further in view of Croce et al. [US 5,633,136(1997)].

Claim 12 is drawn to an embodiment of Claim 11 wherein the cancer is caused associated parasitic infectious agent selected from a defined group which includes *P. falciparum*..

Carson et al. teach all of the limitations of Claim 8 except these authors do not explicitly teach detecting the nucleic acid of the parasitic infectious agent *P. falciparum.* However, as evidenced by Wataya et al. it was well known in the art at the time of the invention to detect *P. falciparum* nucleic acids in a biological sample using PCR and probes specific for the amplified *P. falciparum* nucleic acids. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to detect *P. falciparum* nucleic acids using the primers disclosed by Wataya et al. in the method of Carson et al. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

17. **Claim(s) 13** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson et al. [US 5,747,251 (1998)] as applied to Claim 1 above and further in view of Atlas et al. [US 5,298,392(1994)].

Claim 13 is drawn to an embodiment of Claim 1 wherein said method is used in environmental monitoring, forensics or in food and feed industry mionitoring.

Carson et al. teach all of the limitations of Claim 13 except these authors do not explicitly teach using their method in environmental monitoring. However, as evidenced by Atlas et al. it was well known in the art at the time of the invention to use PCR and probes to detect *the* nucleic acids of potentially pathogenic organisms in a biological sample using PCR and probes specific for the amplified nucleic acids derived from pathogenic organisms in a biological sample. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the method of Carson et al. for environmental monitoring as suggested by Atlas et al. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

18. **Claim(s) 20** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. [US 6,060,288 (2000)] as applied to Claim 1 above and further in view of Virtanen [US 6,566,069 (2003)].

Claim 20 is drawn to an embodiment of Claim 1 wherein the linking agent comprises a polyethylene glycol spacer.

Adams et al. teach all of the limitations of Claim 20 except these authors do not explicitly teach using a linking agent comprising a polyethylene glycol spacer. However, as evidenced by Virtanen et al. the use of a linking agent comprising a polyethylene glycol spacer to attach oligos to a solid support was well known at the time of the invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Adams et al. wherein the linking agent comprises a polyethylene glycol spacer. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will

perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

19. **Claim(s) 20** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson et al. [US 5,747,251 (1998)] as applied to Claim 1 above and further in view of Virtanen [US 6,566,069 (2003)].

Claim 20 is drawn to an embodiment of Claim 1 wherein the linking agent comprises a polyethylene glycol spacer.

Carson et al. teach all of the limitations of Claim 20 except these authors do not explicitly teach using a linking agent comprising a polyethylene glycol spacer. However, as evidenced by Virtanen et al. the use of a linking agent comprising a polyethylene glycol spacer to attach oligos to a solid support was well known at the time of the invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Carson et al. wherein the linking agent comprises a polyethylene glycol spacer. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

20. **Claim(s) 20-21** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. [US 6,060,288 (2000)] as applied to Claim 1 above and further in view of Kurz et al. [US 6,429,300 (2002)].

Claim 20 is drawn to an embodiment of Claim 1 wherein the linking agent comprises a polyethylene glycol spacer.

Adams et al. teach all of the limitations of Claim 20 except these authors do not explicitly teach using a linking agent comprising a polyethylene glycol spacer. However, as evidenced by Kurz et al. the use of a linking agent comprising a polyethylene glycol spacer to attach oligos to a second substance

was well known at the time of the invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Adams et al. wherein the linking agent comprises a polyethylene glycol spacer. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Claim 21 is drawn to an embodiment of Claim 20 wherein the polyethylene glycol spacer is selected from a defined group which includes triethylene glycol spacer.

Kurz et al. teach this limitation see, at least for example, Claim 26.

21. **Claim(s) 20-21** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson et al. [US 5,747,251 (1998)] as applied to Claim 1 above and further in view of Janjic et al. [US 6,582,918 (2003)].

Claim 20 is drawn to an embodiment of Claim 1 wherein the linking agent comprises a polyethylene glycol spacer.

Carson et al. teach all of the limitations of Claim 20 except these authors do not explicitly teach using a linking agent comprising a polyethylene glycol spacer. However, as evidenced by Janjic et al. the use of a linking agent comprising a polyethylene glycol spacer to attach oligos to a another substrate was well known at the time of the invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Carson et al. wherein the linking agent comprises a polyethylene glycol spacer. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Claim 21 is drawn to an embodiment of Claim 20 wherein the polyethylene glycol spacer is selected from a defined group which includes hexaethylene glycol spacer.

Janjic et al. teach this limitation.

22. **Claim(s) 28 and 37** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. [US 6,060,288 (2000)] as applied to Claim 1 above and further in view of Monks et al. [US 6,022,700 (2000)].

Claim 28 is drawn to an embodiment of Claim 1 wherein the solid substrate is selected from a defined group which includes wells.

Claim 37 is drawn to an embodiment of Claim 28 wherein the solid substrate is a microwell suitable for use in quantitative assays that employ direct fluorescence detection.

Adams et al. teach all of the limitations of Claim 28 and 37 except these authors do not explicitly teach using a solid substrate which comprises wells. However, as evidenced by Monks et al. the use of solid substrates comprising wells (i.e. microwells) in a biological assays utilizing direct fluorescence detection was well known in the art at the time of the invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Adams et al. wherein the solid substrate comprises wells. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

23. **Claim(s) 37** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson et al. [US 5,747,251 (1998)] as applied to Claims 1 and 28 above and further in view of Monks et al. [US 6,022,700 (2000)].

Claim 37 is drawn to an embodiment of Claim 28 wherein the solid substrate is a microwell suitable for use in quantitative assays that employ direct fluorescence detection.

Carson et al. et al. teach all of the limitations of Claim 37 except these authors do not explicitly teach that their method employs direct fluorescence detection. These authors do teach using microtiter plate like those used in ELISA and fluorescent labels to detect the primer extension products covalently attached to the solid support. Again it must be pointed out that these authors do not teach that their method employs direct fluorescence detection. However, as evidenced by Monks et al. the use direct fluorescence detection in an assay comprising the use of microwell plates was well known in the art at the time of the invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Carson et al. wherein direct fluorescence detection is utilized. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

24. **Claim(s) 38-39** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. [US 6,060,288 (2000)] as applied to Claim 1 above and further in view of George Jr. et al. [US 5,728,526 (1998)].

Claim 38 is drawn to an embodiment of Claim 1 wherein said extending is carried out in an extension mixture comprising dATP, dCTP, dTTP, dGTP, dITP, dUTP and a polymerizing agent.

Adams et al. teach all of the limitations of Claim 38 except these authors do not explicitly teach performing the extension reaction using an extension mixture comprising dATP, dCTP, dTTP, dGTP, dITP, dUTP. However, as evidenced by George Jr. et al. - see Column 13, beginning at line 5, the use of an extension mixture comprising dATP, dCTP, dTTP, dGTP, dITP, dUTP, while uncommon, was known in the art at the time of the invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Adams et al. wherein the extension mixture comprising dATP, dCTP, dTTP, dGTP, dITP, and dUTP. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Claim 39 is drawn to an embodiment of Claim 38 wherein the polymerizing agent is selected from a defined group which includes Taq DNA polymerase.

George Jr. et al. teach this limitation, see, at least for example, Column 13, beginning at about line 33.

25. **Claim(s) 38-39** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson et al. [US 5,747,251 (1998)] as applied to Claim 1 above and further in view of George Jr. et al. [US 5,728,526 (1998)].

Claim 38 is drawn to an embodiment of Claim 1 wherein said extending is carried out in an extension mixture comprising dATP, dCTP, dTTP, dGTP, dITP, dUTP and a polymerizing agent.

Carson et al. teach all of the limitations of Claim 38 except these authors do not explicitly teach performing the extension reaction using an extension mixture comprising dATP, dCTP, dTTP, dGTP, dITP, dUTP. However, as evidenced by George Jr. et al. - see Column 13, beginning at line 5, the use of an extension mixture comprising dATP, dCTP, dTTP, dGTP, dITP, dUTP, while uncommon, was known in the art at the time of the invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Carson et al. wherein the extension mixture comprising dATP, dCTP, dTTP, dGTP, dITP, and dUTP. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Claim 39 is drawn to an embodiment of Claim 38 wherein the polymerizing agent is selected from a defined group which includes Taq DNA polymerase.

George Jr. et al. teach this limitation, see, at least for example, Column 13, beginning at about line 33. Carson et al. teach using Taq DNA polymerase and/or Pyroccocus DNA polymerase

26. **Claim(s) 42** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. [US 6,060,288 (2000)] as applied to Claims 1 and 41 above and further in view of McMillian [US 6,312,929 (2001)].

Claim 42 is drawn to an embodiment of Claim 41 wherein the label is a fluorescent dye selected from a defined group which includes fluorescein.

Adams et al. teach all of the limitations of Claim 42 except these authors do not explicitly teach that the label is a fluorescent dye selected from a defined group which includes fluorescein. However, as evidenced by McMillian the use of fluorescein as a fluorescent label was well known in the art at the time of the invention. See at least for example Column 13, beginning at about line 7. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Adams et al. wherein fluorescein is the label on the probe nucleic acid. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

27. **Claim(s) 42** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson et al. [US 5,747,251 (1998)] as applied to Claims 1 and 41 above and further in view of McMillian [US 6,312,929 (2001)].

Claim 42 is drawn to an embodiment of Claim 41 wherein the label is a fluorescent dye selected from a defined group which includes fluorescein.

Carson et al. teach all of the limitations of Claim 42 except these authors do not explicitly teach that the label is a fluorescent dye selected from a defined group which includes fluorescein. However, as evidenced by McMillian the use of fluorescein as a fluorescent label was well known in the art at the time of the invention. See at least for example Column 13, begining at about line 7. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Carson et al. wherein fluorescein is the label on the probe nucleic acid. Absent an unexpected result, the substitution of one well known method/reagent with known properties for a second well known method /reagent with known properties is routine in the art. As

regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

CLAIM OBJECTIONS

28. **Claim(s) 18-19, 22-27 and 30-36** is/are objected to because it/they is/are dependent upon a rejected independent base claim.

CONCLUSION

29. **Claim(s) 1-42** is/are rejected and/or objected to for the reason(s) set forth above.

30. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (703) 308-6567. The examiner can normally be reached Monday-Friday from 8:30AM -5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

The fax number for this Examiner is (703) 746-8465. Before faxing any papers please inform the examiner to avoid lost papers. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989). Any inquiry of a general nature or relating to the status of this application should be directed to the group receptionist whose telephone number is (703) 308-0196.

♦Please note that the USPTO is scheduled to relocate to its new home in Alexandria, VA very soon (JAN 04'). As a result, t he examiner's telephone and desktop FAX numbers will be changing. The new telephone and desktop FAX numbers for Ethan Whisenant, Ph.D. are/will be as shown below:

New Telephone number : (571)272-0754

New FAX number : (571)273-07

ETHAN WHISENANT
PRIMARY EXAMINER